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Hambrecht & Quist

Magainin Ready For Phase III Trial

By Brenda Sandburg
News Editor

Magainin Pharmaceuticals Inc. plans to begin a Phase III comparative trial of its lead product, MSI-78, in diabetic patients in late spring. The trial will consist of four treatment arms: MSI-78 once a day, MSI-78 twice a day, SmithKline Beecham's Bactroban and systemic erythromycin.

Jay Moorin, Magainin's president and chief executive officer, said Tuesday at the Hambrecht & Quist Annual Life Sciences Conference in San Francisco that the company will study MSI-78 for treatment of lower-extremity infections in diabetics (which involve Gram-negative bacteria) to get the broadest labeling for the drug.

The topical anti-bacterial and anti-fungal drug is currently in a Phase IIb/III trial for treating impetigo, which is caused by Gram-positive organisms. Magainin

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Mice Produce EPO in Gene Therapy Study

By Brenda Sandburg
News Editor

Mice that received implants of skin cells modified to contain the erythropoietin gene have produced therapeutic levels of EPO for one year, Transkaryotic Therapies Inc. reported Wednesday at Hambrecht & Quist's Annual Life Sciences Conference.

TKT of Cambridge, Mass., is continuing the experiments to determine whether the gene therapy will last the entire lifetime of the animals. Such a therapy could replace the weekly injections of genetically engineered EPO that are given to patients with chronic anemia caused by kidney disease. TKT said the annual cost of such treatment — which is often lifelong — is approximately $6,000 per year.

EPO is currently marketed by Amgen Inc. for treatment of chronic anemia. Johnson & Johnson licensed it from Amgen for all indications except use in kidney dialysis. TKT's president and chief executive officer, Michael Forrest, said TKT would have been unable to commercialize the

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Elanex Challenges Amgen's EPO Patent

By Karl A. Thiel
Associate Editor

Amgen Inc. is once again facing legal claims against its patent on recombinant human erythropoietin (EPO). This time the challenge comes from Elanex Pharmaceuticals Inc., a privately held company based in Bothell, Wash., that markets its own version of EPO in countries outside the U.S.

Amgen (NASDAQ:AMGN) of Thousand Oaks, Calif., filed suit against Elanex and its licensees on Oct. 26, 1993, in Seattle District Court, claiming that Elanex was violating Amgen's U.S. EPO patent by exporting host cells necessary for the production of the recombinant hormone. Amgen's patent on EPO, used to treat anemia associated with renal disease, expires Oct. 27, 2004.

In a Dec. 16, 1993, answer and counterclaim, Elanex stated that its current operations do not infringe the Amgen patent, and that Amgen's EPO patent is invalid. Although Elanex has not yet filed its formal arguments against Amgen, the company stated that it will oppose Amgen's patent on the grounds that the two EPO technologies and EPO products are distinctly different.

In March 1991 the U.S. Court of Appeals for the Federal Circuit ruled that Amgen's patent was valid and enforceable, and was infringed by Genetics Institute's EPO patent.

According to an Elanex document describing its current patent litigation strategy, the company believes the 1991 decision in *Amgen v. Chugai Pharmaceutical Co. Ltd.* (GI's marketing partner) restricts Amgen's U.S. patent to cover "only those variant forms of EPO that were actually taught in the patent." GI lost its challenge to Amgen's EPO business because GI was producing the

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Hambrecht & Quist

Matrix Begins Phase II Trials On Prostate Cancer Drug

Matrix Pharmaceuticals Inc. has initiated Phase II trials of its injectable therapeutic implant for the treatment of prostate cancer, Craig McMullen, the company's president and chief executive, announced Wednesday at the Hambrecht & Quist Annual Life Sciences Conference in San Francisco.

The injectable gel delivers a local, controlled-release dose of 5-fluorouracil (5-FU) to cancerous prostate tissue. The drug is delivered in a biodegradable protein matrix, which controls the rate of drug release, along with a vasoconstrictor to hold the drug in the tissue.

Confirmation of Earlier Study

In what the company is calling a "limited" Phase II study, Matrix (NASDAQ:MATX) of Menlo Park, Calif., will seek histological confirmation of the results from its Phase I/II dose escalation study on the product, initiated in March 1992. Matrix said it expects to conclude enrollment in the Phase I/II trial at the end of this month.

In the Phase II trial, tumors in about 15 patients scheduled for surgical removal of the prostate will first be injected with three Intradose-FU injection treatments over a period of six weeks. In addition to providing efficacy data, the subsequent excisions will give the company information on drug distribution, safety and intraprostatic dose requirements. Matrix said it hopes to move to Phase III trials in 12 to 15 months.

Matrix is developing Intradose injection products for cancers of the liver and head and neck, and superficially accessible tumors such as melanoma, recurrent breast cancer and squamous cell carcinoma. Phase I/II trials for the head and neck and liver indications began in early 1992; the accessible tumor protocol was added last August. All three trials concluded enrollment in December and are currently in data analysis. The company plans to go directly into "approval-directed" Phase II/III trials for these three indications in the second half of 1994 in the U.S. and Europe, according to a company representative. — *Karl A. Thiel*

Cytel Completes Phase I

Cytel Corp. has achieved two developmental milestones, the company's president and chief executive, Ty Kranzler, announced Wednesday at the Hambrecht & Quist Annual Life Sciences Conference.

Kranzler said Cytel (NASDAQ: CYTL) of San Diego completed Phase I clinicals on Theradigm-HBV, its hepatitis B vaccine, and has filed an investigational new drug (IND) application for Cylexin, its cell-adhesion product.

The company is now evaluating data from its safety and tolerability study of Theradigm-HBV in healthy volunteers to assess whether the agent can produce specific cytotoxic T cell (CTL) response against the hepatitis B virus. Cytel said it hopes to complete its analysis in the first quarter of this year.

In the second quarter Cytel hopes to move to Phase II trials of Theradigm-HBV to assess the drug's ability to induce CTLs in patients with chronic hepatitis.

Cylexin Trials

Following FDA approval of its IND, the company plans to begin human clinical trials of Cylexin, its carbohydrate-based small-molecule selectin blocker. Cylexin is being developed for the treatment of diseases involving reperfusion injury — tissue damage that occurs when blood flow is restored to tissue that has been ischemic, as in heart attacks, stroke and trauma.

The company said it hopes to move by midyear from a Phase I safety analysis of Cylexin in healthy volunteers to a Phase II assessment of the efficacy of the agent in treating acute lung injury secondary to reperfusion following a pulmonary thromboembolectomy. Subsequent trials will evaluate the ability of Cylexin to prevent reperfusion to the heart following myocardial infarction. — *Karl A. Thiel*

TKT

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EPO gene therapy without obtaining a license to the EPO gene patent from Amgen or J&J. However, he said TKT scientists "have come up with a novel way of activating the existing EPO gene in normal cells in a fashion which absolutely eliminates the need to get a license."

Forrest explained that within the skin fibroblast cell there is a control region — a gene sequence — that tells the cell not to make EPO since EPO is not naturally produced in skin fibroblast cells. He said TKT is able to insert its own control region in the cell that deletes the existing control region. The new control region instructs the cell to produce EPO. In this way, Forrest told *BioWorld*, EPO is activated without using Amgen's patented gene sequence.

TKT is developing gene therapies for several diseases. The company plans to begin clinical trials of human growth-hormone delivery in cancer patients suffering from cachexia (muscle wasting) early this year. TKT also expects to file an investigational new drug (IND) application later in the year for either a Factor VIII gene therapy for hemophilia A or a Factor IX gene therapy product for hemophilia B. ■

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Genetic Maps for Farm Animals

By David C. Holzman
Washington Editor

U.S. Department of Agriculture scientists have developed the first genetic maps for cattle, sheep and swine, Agriculture Secretary Mike Espy announced this week.

The maps, which have been under development since January 1992, each contain several hundred markers and are based on a combined total of more than 100,000 genotypes, Craig Beatty told *BioWorld*. He is the leader of the Gene Mapping Group at the Agricultural Research Service's Meat Animal Research Center in Clay Center, Nebraska.

Researchers will use the markers as the basis to link economically useful traits such as disease resistance, leanness or tenderness.

The maps will be accessible to outside researchers through an on-line data base beginning in March. "It's an interactive data base that allows an investigator to access raw data rather than compile data," said Beatty. For example, an outside investigator could use the data base to help determine the position of a structural gene.

As useful genes are filled in, it will become possible to determine the genotype of the animals so ranchers can improve breeding. "But you've got to have biotechnology companies that can do the testing and have the probes for the livestock industry, or you will never get the technology implemented," Dan Laster, the center's director, told *BioWorld*. ■

Magainin

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(NASDAQ:MAGN) of Plymouth Meeting, Pa., expects to meet with FDA after this trial is completed in March.

MSI-78 is the first of the company's synthetic magainins to enter clinicals. In a Phase II trial, the drug was able to reduce the number of bacteria and fungi present in a skin infection by three to four orders of magnitude within one hour (see *BioWorld*, July 9).

Magainins, a family of peptide compounds isolated from frog skin, are able to kill a wide variety of pathogenic microorganisms. Moorin said MSI-78 is the broadest-spectrum antibiotic discovered to date. He said pathogens are becoming increasingly resistant to antibiotics and noted a lack of new classes of antibiotics under development. The company has not observed resistance to the magainins, Moorin said.

Moorin said Magainin will probably try to prove MSI-78's efficacy against a broad spectrum of microorganisms before seeking FDA approval. Bactroban, a treatment for impetigo, is the only topical wide-spectrum antibiotic on the market.

Magainin is developing several other magainin compounds for topical and ophthalmic usage, including MSI-420 for corneal wound healing, MSI-404 for disinfecting contact lenses and MSI-469 for use as a mouthwash or toothpaste to treat periodontal disease. Magainin developed the latter product under an agreement with Colgate-Palmolive. Moorin said at H&Q that Colgate has until November to decide whether it will pursue an IND filing or return the drug to Magainin.

Moorin said Magainin has tested more than 380 compounds under its agreement with Sandoz to develop systemic anti-cancer products (see *BioWorld*, Dec. 29, 1992).

Sexually Transmitted Diseases

Magainin's executive vice president and chief operating officer, Leonard Jacob, also noted that the company is working with the National Institutes of Health's contraceptive branch to test magainins for use as topical microbicides against sexually transmitted diseases. The company has supplied NIH with different classes of magainins. Jacob said a magainin mimetic, MSI-753, is able to kill a variety of bacteria and fungi upon contact.

During a break-out session at H&Q, Moorin said the company has been able to reduce manufacturing costs of MSI-78 by working with Abbott Labs. "To make a gram of amino acid peptide in solid phase costs $700 per gram," Moorin said. To make the same gram in a scaled-up solution process, as Abbott is doing, costs in the range of $35-120, he said. Using a scaled-up recombinant process will keep costs in the $2-20 range. Jacob noted that Magainin is working with a European-based manufacturer to use a recombinant manufacturing process. ■

Corange Completes Private Placement

Corange Ltd. announced that it has raised $300 million from the private placement of senior notes that are due in the years 2002/2008. The Deutsche Bank AG London arranged the transaction and Metropolitan Life Insurance Co. and the Prudential Insurance Co. of America provided the funding.

In the past three months, privately held Corange of Hamilton, Bermuda, has invested almost $300 million in two biotechnology companies. In October, Corange invested $75 million in Protein Design Labs Inc. and in December it signed a deal with CellPro Inc. to invest up to $220 million (see *BioWorld*, Dec. 7).

EPO

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same EPO as Amgen and not an analog, the document states.

"There are strong arguments for narrowing the scope of coverage of Amgen's patent," it continues. "This is necessarily so because Elanex came along with a superior variant EPO which was never contemplated nor taught in the Amgen patent. Our EPO is the case that demonstrates that the Amgen patent is overly broad."

Elanex's director of international operations, Gregory Barker, told *BioWorld* that Elanex's EPO is derived from baby hamster kidney cells, while Amgen's comes from Chinese hamster ovary cells. He also said Elanex's product differs from Amgen's in molecular weight and protein structure, and is taken from a different gene fragment. Elanex's strategy document further states that it "can prove that Elanex EPO is both structurally and chemically different from Amgen EPO. It is more potent and has less side effects than Amgen EPO."

Elanex Claims Amgen Agreed not to Interfere

Elanex's Dec. 16 counterclaim also charges that Amgen "agreed that so long as Elanex engaged in EPO activities outside of (the U.S.), neither Amgen nor its licensees would take any action to interfere with Elanex's non-USA activities."

Elanex announced last week that will seek to market the drug in the U.S. if it can gain a favorable court decision. The company has retained Northwest Capital Inc. to pursue licensing agreements with U.S. pharmaceutical companies. Elanex's largest current market for EPO is in India; the company also sells its product or has licensing agreements with companies in Argentina, South Africa, Korea, Germany and several Latin American countries.

Elanex will also dispute Amgen's infringement claim, arguing that its licensees are in accordance with the patent laws of their respective countries and that its own domestic activities do not constitute infringement.

Amgen would not comment on the litigation.

Elanex also is currently opposing European patents to EPO held by Amgen and GI. Elanex, like the other two companies, holds a patent to EPO granted by the European Patent Office. The company also has patents for its EPO product in Australia, Portugal, Sri Lanka and Switzerland. Elanex has applied for patents in Brazil, Canada, China, Denmark, Finland, Japan, Mexico, Norway, the Philippines and the U.S.

In Europe, the company has mapped out several potential litigation strategies. With the European Patent Office, the strategy document states, Elanex can only seek to have Amgen's "very broad" patent invalidated. The company is considering several different courses in individual European countries, however. "We can move to have the Amgen patent revoked or restricted so that our patents co-exist," the document states.

Alternatively, it continues, Elanex could seek compulsory licensing in countries where Amgen is unwilling to enter into voluntary licensing agreements or "we can prove that our EPO is noninfringing," it concludes.

Elanex was founded in 1984. The company's only product is its recombinant human EPO, which it licensed from the University of Washington in the mid-1980s. ■

Scios Nova Begins Clinicals on Natrecor

Scios Nova announced Wednesday that it has begun Phase I/II clinical studies of Natrecor, its human brain natriuretic peptide (hBNP) for the treatment of acute congestive heart failure.

The study will include 40-60 heart failure patients at several sites in the U.S. Scios Nova (NASDAQ:SCIO) of Mountain View, Calif., filed an investigational new drug application with FDA last November.

The company's lead compound, Auriculin ANP, is in a 500-patient Phase III trial for the treatment of acute kidney failure.

Jackson Leaves Telios

Robert Jackson has resigned as president and chief executive officer of Telios Pharmaceuticals Inc. for health reasons. He will remain a member of the San Diego company's board of directors. Theodor Heinrichs has reassumed the position of CEO until a successor can be found.

Correction

An article in the Jan. 6 issue of *BioWorld* concerning Telor Ophthalmic Pharmaceuticals should have specified that the company will develop an eye-dropper formulation of ethacrynic acid as well as a new class of molecules with similar properties.

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